REMARKS

1. Claim Amendments

Claims 1-10 and 19-25 are currently pending. Applicants have canceled claim 18. Claims 4 and 10 are withdrawn from consideration. All amendments are made without prejudice to filing a continuation/divisional application directed to the canceled subject matter. No new matter is added by the amendments.

2. New Ground of Rejection

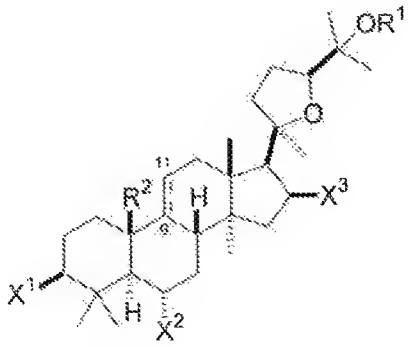
Claim 18 stands rejected as depending from a cancelled claim. Applicants have cancelled claim 18 without prejudice. Withdrawal of this rejection is respectfully requested.

3. Rejection under 35 U.S.C. 103(a)

Claims 1-3, 5-9, 18-25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mousa (U.S. Patent no. 6,171,604) in view of Chou (U.S. Patent No. 6,855,344 or Chou (US Pub. No. 2003/0108629, Pub Date July 12, 2003, filed July 16, 2002) as evidenced by Papadopoulos et al. (JAOCS), Close (U.S. Pre-grant publication No. 2002/0044977) and Wu (U.S. Patent no. 6,696,094).

A. Claims

Independent claim 1, on which claims 2-3, 5-8 and 17-25 are dependent, is directed to a method for conditioning the skin, comprising: applying topically to the skin a formulation comprising an isolated compound of formula 1:



where:

each of X^1, X^2, and X^3 is independently selected from hydroxy, lower alkoxy, lower acyloxy, keto, and a glycoside;

OR^1 is selected from hydroxy, lower alkoxy, lower acyloxy, and a glycoside;

wherein any of the hydroxyl groups on said glycoside may be substituted with a further glycoside, lower alkyl, or lower acyl, such that the compound includes a maximum of three glycosides; and

R^2 is methyl and ---- represents a double bond between carbons 9 and 11; or, R^2 forms, together with carbon 9, a fused cyclopropyl ring, and ---- represents a single bond between carbons 9 and 11;

wherein the concentration of said compound in said formulation is from 0.01 to 5% (w/v); and wherein said formulation further comprises an ingredient selected from the group consisting of an emulsifier, a surfactant, a thickener, a skin emollient, and a lubricant, and an ingredient selected from the group consisting of a preservative, and an antioxidant.

B. The Office Action Position

The Office Action states that Mousa teaches the application of honey for topical treatment of the skin including skin infections. In one preferred embodiment Mousa allegedly teaches that said composition comprises olive oil, glucose sesquiistearate, methyl glucose dioleate and honey (col. 6, ex 11). The Office states that olive oil is known to comprise antioxidants (Papadopoulos, pg 671). Glucose sesquiistearate and methyl glucose dioleate are allegedly taught by Mousa to be emulsifiers (col. 5, lines 60-62). The Examiner states the honey is known to be an emulsifier in topical compositions (Close, para 0012-0013). (Office Action, page 4)

The Office Action states that Mousa fails to directly disclose a composition comprising Applicant's elected species cycloastragenol, the amount in which said cycloastragenol is present or that the composition has telomerase activity or reconfluence. (Office Action, page 4)

The Office states that Chou teaches that an extract of *Radix astragali* can be used as a topical composition for relief of skin infection. (Office Action, page 5) The Office Action states that it is not relying on Chou for the final 9-herb composition taught by Chou but rather for the teaching that *Radix astragali* relieves skin infection. (Office Action, Page 5). It is allegedly

further taught in Chou that one of the major ingredients of the extract of *Radix astralgali*, astragaloside, is present in an amount of 0.365%. (Office Action, Page 5) The Office states that Wu evidences that cycloastragenol is also a major ingredient of *Radix astragali*. (Office Action, page 6)

The Office alleges that it would have been obvious to utilize the extract of *Radix astragali* in the invention of Mousa. The Office alleges that one would be motivated to utilize the extract of *Radix astragali* since *Radix astragali* is taught as being useful for relieving skin infections, and the composition of Mousa is also taught as being useful for skin infections (Office Action, page 3). It is allegedly prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose. The Office states that there would be a reasonable expectation of success in the combination since Mousa and Chou are teaching compositions that are useful for treating skin infections.

The Office Action states that the composition of Mousa as modified by either Chou reference would necessarily have the same telomerase activity and cell reconfluence properties of instant claims 23 and 24. Since the composition of Mousa in view of either Chou reference allegedly teaches similar, if not the same components, it is the position of the Examiner that the properties of the composition would also be similar. Thus claiming a new use, new function or unknown property which is allegedly inherently present in the prior art does not necessarily make the claim patentable.

C. Applicants response

Applicants submit that the Examiner has failed to apply the proper legal standard for comparing the present invention to the cited references.

An obviousness inquiry is controlled by the factors articulated by the Supreme Court in *Graham v. John Deere Co. of Kansas City* 383 US1 (1966) including 1) the scope and content of the prior art; 2) the differences between the prior art and the claims; 3) the level of ordinary skill in the pertinent art; and 4) objective evidence of nonobviousness. In addition, a long line of Federal Circuit decisions has established that a patent claim is only proved obvious if the prior art, the problem's nature or the knowledge of a person of ordinary skill in the art provide motivation or suggestion to combine the prior art teachings (the 'teaching or suggestion or

motivation" or "TSM test"). While the Supreme Court has recently rejected a rigid application of the TSM test, it stated that the Graham Deere factors still control an obviousness inquiry. *See KSR Int'l Co. v. Teleflex Inc.* 127 S. Ct. at 1727. Moreover, the Court indicated that there is "no necessary inconsistency between the idea underlying the TSM test and the Graham analysis" KSR 127 S.Ct. at 1731. The Court specifically acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. As long as the test is not applied as a 'rigid and mandatory" formula, that test can provide "helpful insight" to an obviousness inquiry.

The Cited Art

The cited reference Mousa includes a honey formulation for topical application. The preparation includes the unaltered active constituents of honey, which provide the preparation with its therapeutic, cosmetic and nutritional benefits. The preparation can be used to treat skin conditions. In some examples, the honey is mixed with olive oil (Example 1). The honey may be also mixed with emulsifiers such as sorbitan sesquiistearate (Example 2). Mousa does not teach or suggest the use of the compounds of the present invention for the treatment of skin.

The cited references Chou (US Pub 2003/0108629) and Chou US 6,855,344 describe compositions including "an aliquot of the herb *Herba epimidii*" and "an aliquot of at least three supplemental herbs" which are selected from a group of eight herbs, one of which is *Radix astragali*. The reference teaches that these multi-herb compositions should be administered for "treatment of various kidney disorders or the promotion of kidney health and to the overall health of the kidney", including "treatment of prostate cancer, prophylactic prostate health, reduction of polyuria, incontinence, proteinuria, as well as for sexual satisfaction" (Abstract) The Office Action states that it is not relying on Chou for the final composition of Chou but rather for the teaching that *Radix astragali* relieves skin infection. (Office Action, page 6).

The cited reference Wu teaches pharmaceutical compositions in the form of intravenous injections and oral capsules for treating patients with HIV infection. The pharmaceutical composition contains 14 ingredients (herbs), including *Radix astragali*.

Applicants traverse the rejection for obviousness for the following reasons.

In this case, the invention is directed to a method for conditioning the skin comprising applying topically to the skin a formulation comprising an isolated compound of formula I wherein the concentration of said compound in said formulation is from 0.01 to 5% (w/v); and wherein said formulation further comprises an ingredient selected from the group consisting of an emulsifier, a surfactant, a thickener, a skin emollient, and a lubricant and an ingredient selected from the group consisting of a preservative and an antioxidant.

There is no teaching in either the Mousa reference, the Chou references or the Wu reference or the Papdopoulos reference or the Close reference to combine the honey composition of Mousa with the R*adix astragali* extract of Chou. The Mousa reference, the Papadopoulos reference and the Close reference are silent with regard to the compounds of formula I or extracts from *Radix astragali*. The Chou references or the Wu reference do not teach the use of extracts of *Radix astragali* for topical application

The Mousa reference teaches away from the combination in part because Mousa states that "it is the active constituents [of honey] that provide the preparation with its therapeutic, cosmetic and nutritional benefits." One of skill would not have any motivation to add any additional ingredients to the honey composition to improve its skin conditioning properties. Absent a teaching or suggestion in the art to combine the compositions, the claimed invention is not obvious. The Office Action states that the honey composition of Mousa may act as an emulsifier (See Close) (Office Action, page 3). Even if the honey composition of Mousa does act as an emulsifier, there is no teaching in Mousa to add the claimed compounds of formula I to the honey composition.

Chou also does not provide any teaching to combine the references. There is no teaching in Chou to use the R*adix astragali* extract in a topical application. Furthermore, there is no teaching in Chou to add to the R*adix astragali* extract an ingredient selected from the group consisting of an emulsifier, a surfactant, a thickener, a skin emollient, and a lubricant, and an ingredient selected from the group consisting of a preservative, and an antioxidant.

Wu also does not provide any teaching to combine the references. There is no teaching in Wu to use the R*adix astragali* extract in a topical application. Furthermore, there is no teaching in Wu to add to the R*adix astragali* extract an ingredient selected from the group

consisting of an emulsifier, a surfactant, a thickener, a skin emollient, and a lubricant, and an ingredient selected from the group consisting of a preservative, and an antioxidant.

The Office Action states that Chou clearly teach the composition of Chou which comprises the extract of Radix astragali for topical application (See Chou col. 22, lines 1-5)

The Chou references are primarily directed to the invention of a 9 herb composition. The references only discuss the properties of the *Radix astragali* extract where they list a variety of traditional Chinese uses for the R*adix astragali* root. First, these uses discuss use of the root and not the use of the extract. Secondly, these uses are vague and conflicting. Thirdly, there is no description of how such conditions are treated with the root. Furthermore, the next paragraph of Chou states that it is safe to take the root orally in moderate amounts. There is no statement of the topical application of the root in Chou.

Secondly, the part of the specification referred to by the Office as support for topical administration is located in a portion of the specification entitled "Composition". That portion of the specification begins by stating that the "composition of the ingredients described can improve the overall benefit and/or effect of each of the ingredients individually.... Instead of simply treating one ailment such as an infection, the 9-herb composition can act" (col. 21, lines 34-40). It goes on to state that extracts of [9 herbs listed] may be mixed in a 9:2:2:2:1:1:1:1:1 ratio and made into capsule form (the 9-herb composition). Col. 21, line 45-55.

Chou is not teaching the topical application of the isolated root extract. Accordingly, there is no teaching or suggestion in Chou of how much of the root to take or of how to make the root into a topical solution. The Chou references do not teach or suggest the topical use of the extract for skin conditioning. One of skill, given this disclosure, would not consider the topical use of the extract for skin conditioning. Furthermore, one skilled in the art would not necessarily have taken from this recitation in Chou that any particular isolated component of *Radix astragali* could be used for skin conditioning. Any one of many components of the root could have been responsible for the disclosed effects of *Radix astragali* recited in Chou.

The Office Action states that though both Chou references are silent as to the amount of cycloastragenol which is preferred, both Chou references do teach a preferred amount of astragaloside specifically 0.365%. The Office Action states that given that astragaloside and

cycloastragenol are both evidenced in Wu to be major ingredients of *radix astragali*, it is the position of the Examiner that the 0.365% would be a starting value which one would look to for the amount of cycloastragenol. Said amount would allegedly be readily optimized by adding more or less extracted *Radix astragali*.

Applicants agree that Chou teaches that the extract of R*adix astragali* contains 0.365% of astragaloside. (Table III). Chou does not state what type of astragaloside is present in that amount or whether that amount is a combination of all of the astragalosides. As described in Kitigawa (Chem. Phar. Bull. 31(2) 698-708, previously made of record) there are at least 11 different astragalosides present in the extract of R*adix astragali*. Accordingly, one of skill in the art, given the Chou references could not be certain that the extract would contain 0.365% (0.00365 mg of a particular astragaloside/mg of extract). Furthermore, applicants have amended claim 1 to recite that the concentration of the compound is from 0.01 to 5% (w/v) or 0.1 mg/ml to 5 mg/ml. The *Radix astragali* extract does not meet this concentration.

Secondly, contrary to the position of the Office, one cannot increase the percentage of a compound in a root extract by adding more root extract. Adding two extracts, each having a concentration of 0.365% will result in a root extract still having a concentration of 0.365%.

A claim limitation is inherent in the prior art if it is necessarily present in the prior art, not merely probably or possibly present. *Akamai Technologies v. Cable & Wireless Internet Services, Inc.* 344 F.3d 1186, 68 USPQ 2d 1186. Applicants note that there is uncertainty that cycloastragenol is a component of the extract of *Radix Astragali*. Applicants had previously pointed out that the Kitigawa reference (*Chem. Pharm. Bull.* 31(2): 689-697, of record) states that cycloastragenol is prepared by hydrolysis of native components of the root. Accordingly, cycloastragenol is not necessarily present in the extract of *Radix astragali*. None of the other isolated compounds now recited in Applicants' claim 25 are reported to be components of *Radix astragali*. As described in the applicants' specification at page 21, line 20 to page 22, line 5, these compounds are prepared synthetically. Clearly, isolated cycloastragenol and the other compounds of claim 25 are not necessarily present in the extract of Chou.

Furthermore, the biological activity reported in Chou teaches away from the claimed invention. A *prima facie* case of obviousness can be rebutted by a showing that the art in any

material respect taught away from the claimed invention *In re Geisler* 116 F.3d 1465, (Fed. Cir. 1997) citing *in re Soni* 54 F.2d 746, 750 (Fed. Cir. 1995).

In treatment of prostate cancer as emphasized by Chou, the desired effect is shown to be inhibition of cell growth, the opposite of the biological effect shown by the applicants. See the Examples of Chou using the 9-herb composition which contains the *Radix astragali* extract, e.g. at paragraphs [0222] (a 30% reduction in cell growth", a significant reduction in cell proliferation"); [0226] ("induction of apoptosis in treated cells"); [0235] ("proliferation of these cells was significantly inhibited"; "85% reduction in cell proliferation") etc. The biological activity touted by the reference is in direct contrast to the benefits obtained by the subject compounds of the applicants' claims as taught by the applicants in the instant application. One skilled in the art, given this disclosure, would not consider that the *Radix astragali* extract would be useful for skin conditioning.

The Office states that this argument is not persuasive because Applicant has not provided any evidence that the Radix component in the Chou composition contributes in any way to the inhibition of cell growth. Applicant is simply referring to the reference supplied by the Office and pointing out that the reference relied on by the Office states that the component reduces cell proliferation. "It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art…A reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered". *Bausch & Lomb v. Barnes-Hind/Hydrocurve* (796 F 2d 443, 230 USPQ 416, Fed. Cir 1986).

A skilled person looking for a method of skin conditioning would not look to a reference focused on inhibiting cell growth for a treatment of prostate cancer. Furthermore, a skilled person would not be motivated to try any possible ingredients in an oral composition for treatment of prostate cancer as a means of skin conditioning and they certainly would not have a reasonable expectation of success.

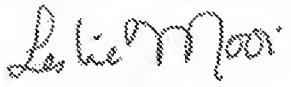
The Papadopoulos et al, Close and Wu references do not cure any of the deficiencies of the Chou or Mousa references.

Accordingly, the combination of Mousa in view of the Chou references as evidenced by Papadopoulos et al, Close and Wu does not make the claimed invention obvious. For these reasons, withdrawal of this rejection under 35 U.S.C. 103(a) is respectfully requested.

Conclusion

In view of the foregoing, the applicants submit that the claims now pending are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

Respectfully submitted



Leslie A. Mooi
Registration No. 37,047

Date: August 5, 2010

Geron Corporation
230 Constitution Drive
Menlo Park, CA 94025